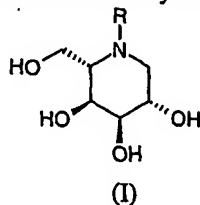


## CLAIMS:

1. A compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof:



wherein

R is  $C_{1-3}$  alkylAr<sup>1</sup> where Ar<sup>1</sup> is phenyl or pyridyl;

wherein phenyl is substituted by one or more substituents selected from CN, CON(R<sup>1</sup>)<sub>2</sub>, SO<sub>2</sub>R<sup>2</sup>, SO<sub>2</sub>N(R<sup>1</sup>)<sub>2</sub>, N(R<sup>5</sup>)<sub>2</sub>, N(R<sup>1</sup>)COR<sup>2</sup>, N(R<sup>1</sup>)SO<sub>2</sub>R<sup>2</sup>, C<sub>0-6</sub> alkylAr<sup>2</sup>, C<sub>2-6</sub> alkenylAr<sup>2</sup> and C<sub>3-6</sub> alkynylAr<sup>2</sup> wherein one or more of the -CH<sub>2</sub>- groups of the alkyl chain may be replaced with a heteroatom selected from O, S and NR<sup>3</sup>, provided, that when the heteroatom is O, at least two -CH<sub>2</sub>- groups separate it from any additional O atom in the alkyl chain; or two adjacent substituents on the Ar<sup>1</sup> phenyl may together form a fused 5- or 6-membered saturated or unsaturated ring wherein the ring optionally contains 1 or 2 heteroatoms selected from O, S and NR<sup>4</sup> and is optionally substituted by one or more substituents selected from, an oxo group, C<sub>1-6</sub> alkyl and C<sub>0-3</sub> alkylAr<sup>4</sup>;

and the Ar<sup>1</sup> phenyl is optionally substituted by one or more additional substituents selected from F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl;

and wherein pyridyl is substituted by one or more substituents, selected from, CN, CON(R<sup>1</sup>)<sub>2</sub>, SO<sub>2</sub>R<sup>2</sup>, SO<sub>2</sub>N(R<sup>1</sup>)<sub>2</sub>, N(R<sup>5</sup>)<sub>2</sub>, N(R<sup>1</sup>)COR<sup>2</sup>, N(R<sup>1</sup>)SO<sub>2</sub>R<sup>2</sup>, F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup>, C<sub>1-6</sub> alkyl, C<sub>0-6</sub> alkylAr<sup>2</sup>, C<sub>2-6</sub> alkenylAr<sup>2</sup> and C<sub>3-6</sub> alkynylAr<sup>2</sup> wherein one of the -CH<sub>2</sub>- groups of the alkyl chain may be replaced with a heteroatom selected from O, S and NR<sup>3</sup>, provided that when the heteroatom is O, at least two -CH<sub>2</sub>- groups separate it from any additional O atom in the alkyl chain; or two adjacent substituents on the Ar<sup>1</sup> pyridyl may together form a fused 5- or 6-membered saturated or unsaturated ring wherein the ring optionally contains 1 or 2 heteroatoms selected from O, S and NR<sup>4</sup> and is optionally substituted by one or more substituents selected from, an oxo group, C<sub>1-6</sub> alkyl and C<sub>0-3</sub> alkylAr<sup>4</sup>;

R<sup>1</sup> is H, C<sub>1-6</sub> alkyl optionally substituted by OH, Ar<sup>3</sup>, or C<sub>1-6</sub> alkylAr<sup>3</sup>, or the group N(R<sup>1</sup>)<sub>2</sub> may form a 5- to 10-membered heterocyclic group optionally containing one or more additional heteroatoms selected from O, S and NR<sup>3</sup> and is optionally substituted by an oxo group;

R<sup>2</sup> is C<sub>1-6</sub> alkyl optionally substituted by OH, Ar<sup>3</sup>, or C<sub>1-6</sub> alkylAr<sup>3</sup>;

R<sup>3</sup> is H, or C<sub>1-6</sub> alkyl;

R<sup>4</sup> is H, C<sub>1-6</sub> alkyl or C<sub>0-3</sub> alkylAr<sup>4</sup>;

R<sup>5</sup> is H, C<sub>1-6</sub> alkyl optionally substituted by OH, Ar<sup>3</sup>, or C<sub>1-6</sub> alkylAr<sup>3</sup>, or the group N(R<sup>5</sup>)<sub>2</sub> may form a 5- to 10-membered heterocyclic group optionally containing one or more additional heteroatoms selected from O, S and NR<sup>3</sup> and is optionally substituted by an oxo group;

Ar<sup>2</sup> and Ar<sup>3</sup> are independently phenyl or a 5- to 10-membered heteroaryl group containing up to 3 heteroatoms selected from O, S and NR<sup>3</sup>, which may be optionally substituted by one or more substituents selected from F, Cl, Br, CN, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl;

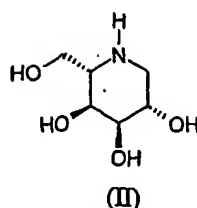
Ar<sup>4</sup> is phenyl or pyridyl either of which may be optionally substituted by one or more substituents selected from F, Cl, Br, CN, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl; and

n = 0, 1 or 2.

2. A compound as defined in claim 1 wherein R is C<sub>1</sub> alkylAr<sup>1</sup>.

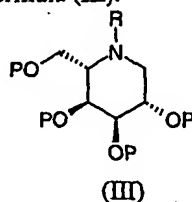
3. A compound as defined in claim 1 or 2 wherein Ar<sup>1</sup> is phenyl, wherein phenyl is substituted as defined for claim 1.
4. A compound as defined in any one of the preceding claims wherein Ar<sup>1</sup> is phenyl, wherein phenyl is substituted by one or more substituents selected from CN, CON(R<sup>1</sup>)<sub>2</sub>, N(R<sup>5</sup>)<sub>2</sub>, and C<sub>0-6</sub> alkylAr<sup>2</sup> wherein one or more of the -CH<sub>2</sub>- groups of the alkyl chain may be replaced with a heteroatom selected from O, S and NR<sup>3</sup>, provided that when the heteroatom is O, at least two -CH<sub>2</sub>- groups separate it from any additional O atom in the alkyl chain, or two adjacent substituents on the Ar<sup>1</sup> pyridyl may together form a fused 5- or 6-membered saturated or unsaturated ring wherein the ring optionally contains 1 or 2 heteroatoms selected from O and NR<sup>4</sup> and is optionally substituted by one or more substituents selected from, an oxo group, C<sub>1-6</sub> alkyl and C<sub>0-3</sub> alkylAr<sup>4</sup>, and the Ar<sup>1</sup> phenyl is optionally substituted by one or more additional substituents selected from F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl.
5. A compound as defined in any one of the preceding claims wherein Ar<sup>1</sup> is phenyl, wherein phenyl is substituted by one or more substituents selected from CN, CON(R<sup>1</sup>)<sub>2</sub>, N(R<sup>5</sup>)<sub>2</sub>, and C<sub>0-6</sub> alkylAr<sup>2</sup> wherein one or more of the -CH<sub>2</sub>- groups of the alkyl chain may be replaced with O, provided that at least two -CH<sub>2</sub>- groups separate it from any additional O atom introduced into the alkyl chain and the Ar<sup>1</sup> phenyl is optionally substituted by one or more additional substituents selected from F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl.
6. A compound as defined in any one of the preceding claims wherein Ar<sup>2</sup> is phenyl which is optionally substituted by one or more substituents selected from F, Cl, Br, CN, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl.
7. A compound as defined in any one of the preceding claims wherein R<sup>1</sup> is H or C<sub>1-6</sub> alkylAr<sup>3</sup>.
8. A compound as defined in any one of the preceding claims wherein R<sup>4</sup> is H or C<sub>1-6</sub> alkyl.
9. A compound as defined in any one of the preceding claims wherein Ar<sup>3</sup> is phenyl which may be optionally substituted by one or more substituents selected from F, Cl, Br, CN, CF<sub>3</sub>, OCF<sub>3</sub>, OR<sup>3</sup> and C<sub>1-6</sub> alkyl.
10. A compound as defined in any one of the preceding claims wherein R<sup>5</sup> is C<sub>1-6</sub> alkyl.
11. A compound of formula (I) as described in any one of Examples 1 to 10 or a pharmaceutically acceptable salt or prodrug thereof.
12. A compound as defined in any one of the preceding claims for use in medicine.
13. A pharmaceutical composition comprising a compound of formula (I) as defined in any one of claims 1 to 11, together with one or more pharmaceutically acceptable carriers, excipients and/or diluents.
14. A process for the preparation of a compound of formula (I) as defined in any one of claims 1 to 11 which comprises:
- a) reductive amination of an aldehyde of formula R<sup>5</sup>CHO wherein R<sup>5</sup> is C<sub>0-2</sub> alkylAr<sup>1</sup> where Ar<sup>1</sup> is as defined in claim 1, with a compound of formula (II):

24



or

b) deprotection of a compound of formula (III):



wherein R is as defined in claim 1 and P, which may be the same or different, are hydroxy protecting groups.

- 10 15. The use of a compound of formula (I) as defined in any one of claims 1 to 11 in the manufacture of a medicament for use as an inhibitor of glucosylceramide synthase.
- 15 16. The use of a compound as defined in any one of claims 1 to 11 in the manufacture of a medicament for the treatment of a glycolipid storage disease.
17. The use as claimed in claim 16 wherein the glycolipid storage disease is Gaucher disease, Sandhoffs disease, Tay-Sachs disease, Fabry disease or GM1 gangliosidosis.
- 20 18. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for the treatment of Niemann-Pick disease type C, mucopolysaccharidosis type I, mucopolysaccharidosis type IIIA, mucopolysaccharidosis type IIIB, mucopolysaccharidosis type VI, mucopolysaccharidosis type VII,  $\alpha$ -mannosidosis or mucopolipidosis type IV.
- 25 19. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for the treatment of cancer in which glycolipid synthesis is abnormal.
- 30 20. The use as claimed in claim 19 wherein the cancer in which glycolipid synthesis is abnormal is selected from, brain cancer, neuronal cancer, neuroblastoma, renal adenocarcinoma, malignant melanoma, multiple myeloma and multi-drug resistant cancer.
- 35 21. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for use in the treatment of Alzheimer's disease, epilepsy, stroke, Parkinson's disease or spinal injury.
22. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for use in the treatment of diseases caused by, infectious microorganisms which utilize glycolipids on the surface of cells as receptors for either the organism itself or for toxins produced by the organism, or infectious organisms for which the synthesis of glucosylceramide is an essential or important process.
- 40 23. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for use in the treatment of diseases associated with abnormal glycolipid synthesis.

24. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for the treatment of a condition treatable by the administration of a ganglioside.

5 25. The use as claimed in claim 24, wherein the condition is treatable by the administration of a GM1 ganglioside.

26. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for use in reversibly rendering a male mammal infertile.

10

27. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for the treatment of obesity.

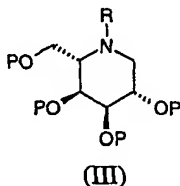
15

28. The use of a compound as defined in any one of claims 1 to 11, in the manufacture of a medicament for the treatment of inflammatory diseases or disorders associated with macrophage recruitment and activation.

20

29. The use as claimed in claim 28, wherein the inflammatory disease or disorder associated with macrophage recruitment and activation is selected from rheumatoid arthritis, Crohn's disease, asthma and sepsis.

30. A compound of formula (III):



25

wherein R is as defined in claim 1 and P, which may be the same or different, are hydroxy protecting groups.